



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Yanagi et al.
Appl. No. : 09/980,559
Filed : May 14, 2002
For : CLONED GENOME OF
INFECTIOUS HEPATITIS C
VIRUS OF GENOTYPE 2A AND
USES THEREOF
Examiner : Li, Bao Q.
Group Art Unit : 1648

DECLARATION UNDER 37 CFR 1.132 OF RAYMOND D. SMITH, Ph.D.

I, Raymond D. Smith, Ph.D., do hereby declare:

1. I am a patent agent employed by the law firm of Knobbe Martens Olson and Bear.
2. I have personal knowledge of the facts set forth below and, if called as a witness, I could and would testify competently thereto.
3. I received a Ph.D. in Biology from the University of California, Irvine. I have over 15 years of expertise in the area of molecular biology.
4. The hepatitis C virus (HCV) genomic RNA type 2a variant identified by Yanagi et al. in the above referenced application and reported as Yanagi et al. 1999 *Virology* **262**:250-263 has a Genbank accession number of AF177036.1 and a corresponding protein ID of AAF01178.1.
5. The previously published HCV genomic RNA type 2a sequence (Okamoto et al. 1991 *J Gen Virol* **72**:2697-2704) has a Genbank accession number of D00944.1.
6. To compare the two HCV type 2a genomic RNA variants at the nucleotide level, I used the NCBI "BLAST 2 SEQUENCES" BLASTN tool to compare the open reading frame

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(ORF) portions of D00944.1 (nt341-9439) and AF177036.1 (nt341-9439). The BLASTN analysis indicated that the ORFs of D00944.1 and AF177036 have 8723 out of 9099 nucleotides that are identical (95.9% identity).

7. To compare the two HCV type 2a genomic RNA variants at the amino acid level, I performed a BLASTX analysis using the ORF portion of D00944.1 (nt341-9439) as a query sequence. The best BLASTX match (excluding self-identification of D00944.1) was a match to protein ID No. AAF01178.1, that corresponds to Accession No. AF177036.1. The ORFs of D00944.1 and AF177036.1 were shown to have 2967 out of 3033 amino acids that are identical (97.8% identity).

8. The percent difference of nucleotide sequences between strain HC-J6 (Okamoto et al., 1991) and strain HC-J6_{CH} **as measured from nucleotide position 341-9439, which corresponds to the ORF**, is **4.1% at the nucleotide level** and the percent difference of predicted amino acid sequence between strain HC-J6 (Okamoto et al., 1991) and strain HC-J6_{CH} is **2.2% at the amino acid level**.

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9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 12-20-04

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